Amendments to the Specification:

Please replace the paragraph beginning at page 4, line 19 with the following amended paragraph:

Figure 1 shows the amino acid and nucleic acid sequence of TGFβ_3 (SEQ ID NO:21 and SEQ ID NO:20);

Please replace the paragraph beginning at page 4, line 20 with the following amended paragraph:

Figure 2 shows the amino acid and nucleic acid sequence of HIF-1α (SEQ ID NO:23 and SEQ ID NO:22);

Please replace the paragraph beginning at page 5, line 34 with the following amended paragraph:

The TGFβ family includes five members, termed TGFβ 1 through TGFβ 5, all of which form homodimers of about 25 kd (reviewed in Massague, 1990). The family also includes TGFβ 1.2 which is a heterodimer containing a β1 and a β2 subunit linked by disulfide bonds. The five TGFβ genes are highly conserved. The mature TGFβ processed cytokines produced from the members of the gene family show almost 100% amino acid identity between species, and the five peptides as a group show about 60-80% identity. The amino acid sequence and nucleic acid sequence of TGFβ_3, are shown in Figure 1 (SEQ ID NO:21 and SEQ ID NO:20) (See also sequences for GenBank Acession Nos. HSTGF31-HSTGF37, and HSTGFB3M).

Please replace the paragraph beginning at page 6, line 23 with the following amended paragraph:

Hypoxia-inducible factor-I (HIF-I) is present in nuclear extracts of many mammalian cells cultivated in a low oxygen atmosphere (Semenza, G.L. et al Mol. Cell. Biol. 12:5447, 1992; Wang, G.L. et al J. Biol. Chem. 268:21513, 1993). HIF-I binds as a phosphoprotein to a short DNA motif (BACGTSSK) (SEQ ID NO:24) identified in the 3 -flanking regions of many hypoxia-induced genes (Semenza, G.L. et al. J. Biol Chem 269:23757, 1994; Liu, Y., et al Circulation Res. 77:638, 1995; Firth, J.D. et al Proc. Natl. Acad. Sci. USA 91:6496, 1994; Abe,

M., et al. Anal. Biochem. 216:276, 1994). HIF-I binds DNA as a heterodimeric complex composed of two subunits of the inducible HIF-1α and the constitutively expressed HIF -Iβ.

Please replace the paragraph beginning at page 12, line 12 with the following amended paragraph:

A substance that regulates trophoblast invasion may be a molecule which interferes with the transcription and/or translation of TGFβ_3, TGFβ receptors, or HIF-1α. For example, the sequence of a nucleic acid molecule encoding TGFβ_3, TGFβ receptors (e.g. endoglin, R-I (ALK-I), R-II, or RI-RII-endoglin complex) or fragments thereof, may be inverted relative to its normal presentation for transcription to produce an antisense nucleic acid molecule. An antisense nucleic acid molecule may be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. Examples of antisense molecules for TGFβ_3 are 5'-CCTTTGCAAGTGCATC-3' (SEQ ID NO:1) and 5'-GATGCACTTGCAAAGG-3' (SEQ ID NO:2).

Please replace the paragraph beginning at page 16, line 14 with the following amended paragraph:

Phosphorothioate oligonucleotides (ON) were synthesized on a DNA synthesizer and purified by capillary electrophoresis. Oligonucleotides of 16 base pairs targeted against sequences adjacent to the AUG initiation codon of human endoglin (23) mRNA were synthesized. Previous studies have demonstrated that antisense oligonucleotides, targeted to sequences adjacent to initiation codons, are most efficient in inhibiting translation (24). Furthermore, 16-mer oligonucleotides are short enough to be taken up efficiently and provide sufficient specificity for hybridization to the corresponding target mRNA (24). The sequences of the antisense and sense endoglin oligonucleotides were 5'-GCGTGCCGCGGTCCAT-3' (SEQ ID NO:3) and 5'-ATGGACCGCGGCACGC-3' (SEQ ID NO:4), respectively. An oligomer with the same composition as the antisense oligonucleotide, but with a scrambled sequence, 5'-GCGGGCCTCGTTCCAG-3' (SEQ ID NO:5), was also synthesized and used as a negative control. Oligonucleotides were dissolved in water and their concentration was estimated by optical density at OD_{260}. Antisense or sense oligonucleotides (5-10 μM) were added to the

villous explants on day 1 and day 3 of culture. EVT sprouting and migration from the distal end of the villous tips were recorded daily for up to 6 days.

Please replace the paragraph beginning at page 21, line 16 with the following amended paragraph:

Total RNA was extracted from the placenta, reverse transcribed and amplified by 15 cycles of PCR using TGFβ isoform specific primers. RT-PCR products were analysed by Southern blotting using ^{32}P-labelled TGFβ cDNAs. The primer set chosen for amplification of TGFβs were based on human mRNA sequences. Primers used for amplification were: (a) TGFβ_1 cNDA: (forward primer): 5'-GCCCTGGACACCAACTATTGCT-3' (SEQ ID NO:6), (reversed primer): 5'-AGGCTCCAAATGTAGGGGC AGG-3' (SEQ ID NO:7) (predicted product size = 161 bp); (b) TGFβ_2 cDNA (forward primer): 5'-CATCTGGTCCCGGTGGCGCT-3' (SEQ ID NO:8), (reversed primer): 5'-GACGATTCTGAAGTAGGG-3' (SEQ ID NO:9) (predicted product size = 353 bp; (c) TGFβ_3 cDNA: (forward primer): 5'-CAAAGGGCTCTGGTGGTCCTG-3' (SEQ ID NO:10), (reversed primer): 5'-CTTAGAGGTAATTCCCTTGGGG-3' (SEQ ID NO:11) (predicted product size = 374 bp); (c) β-actin cDNA: forward primer): 5'-CTTCTACAATGAGCTGGGTG-3' (SEQ ID NO:12), (reversed primer): 5'-TCATGAGGTAGTCAGTCAGG-3' (SEQ ID NO:13) (predicted product size = 307 bp). The identity of the PCR reaction products was also confirmed by sequencing.

Please replace the paragraph beginning at page 21, line 37 with the following amended paragraph:

Villous explant cultures were established as described previously (I. Caniggia et al. *Endocrinology*, 138, 3976 1997, O.Genbacev et al., Placenta 13:439, 1992) from first trimester human placentae (5-10 weeks gestation) or from preeclamptic and age-matched control placentae (30 and 32 weeks of gestation) after collection according to ethical guidelines. The preeclamptic group was selected according to both clinical and pathological criteria (L. Chesley, *Obstet. Gynecol.* 65, 423, 1985). Following an overnight period in serum-free DMEM/F12, explants were cultured in media containing antisense or sense oligonucleotides (10μM) for up to 6 days (with changes of media/oligonucleotides every 48 hours). Phosphorothioate oligonucleotides of

16 base pairs targeted against sequences adjacent to the AUG initiation codon of different human TGFβ isoforms mRNA were synthesized as follows: TGFβ_1 5'-CCCCGAGGGCGGCATG-3' (SEQ ID NO:14) and 5'-CATGCCGCCCTCGGGG-3'(SEQ ID NO:15), respectively; TGFβ_2 5'-CACACAGTAGTGCATG-3' (SEQ ID NO:16) and 5'-CATGCACTACTGTGTG-3' (SEQ ID NO:17); TGFβ_3 5'-CCTTTGCAAGTGCATC-3' (SEQ ID NO:18) and 5'-GATGCACTTGCAAAGG-3' (SEQ ID NO:19).